AD-A132 407 PRIMARY EYE IRRITATION POTENTIAL OF THE HOLSTON COMPOUNDS: VIRGIN DMSO (D..(U) LETTERMAN ARMY INST OF RESEARCH PRESIDIO OF SAN FRANCISCO CA 1/1

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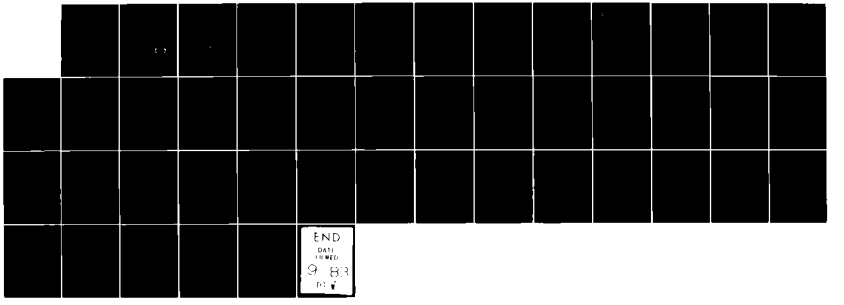

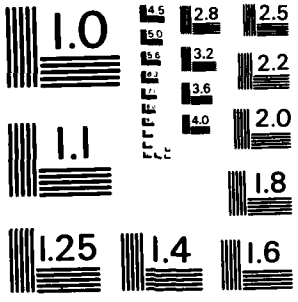

MICROCOPY RESOLUTION TEST CHART
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(12)

INSTITUTE REPORT NO. 155

PRIMARY EYE IRRITATION POTENTIAL OF THE HOLSTON COMPOUNDS:
Virgin DMSO, DMSO Recycle Solvent, and DMSO Evaporator Sludge

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and
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TOXICOLOGY GROUP,
DIVISION OF RESEARCH SUPPORT

AUGUST 1983

Toxicology Series 59

LETTERMAN ARMY INSTITUTE OF RESEARCH
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129

Primary Eye Irritation of the Holston Compounds: Virgin DMSO, DMSO Recycle Solvent, and DMSO Evaporator Sludge (Toxicology Series 59)--Kellner and White

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER LAIR Institute Report 155	2. GOVT ACCESSION NO. AD-A132 407	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Primary Eye Irritation Potential of the Holston Compounds: Virgin DMSO, DMSO Recycle Solvent and DMSO Evaporator Sludge		5. TYPE OF REPORT & PERIOD COVERED Final 10 Feb - 30 Mar 83 6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Thomas P. Kellner, BA, SP4 Craig W. White, DVM, CPT VC		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS US Army Medical Research and Development Command Letterman Army Institute of Research Presidio of San Francisco, CA 94129		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME AND ADDRESS US Army Medical Research and Development Command Fort Detrick Frederick, MD 21701		12. REPORT DATE August 1983 13. NUMBER OF PAGES 38
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office)		15. SECURITY CLASS. (of this report) UNCLASSIFIED 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

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18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Eye Irritation, Holston Compounds, Virgin DMSO, DMSO Recycle Solvent, DMSO Evaporator Sludge

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The primary eye irritation potential of the Holston Compounds (Virgin DMSO*, DMSO Recycle Solvent, and DMSO Evaporator Sludge) was tested by placing these materials in the conjunctival cul-de-sac of rabbit eyes. The study was conducted in compliance with the Good Laboratory Practice Regulations. All of the DMSO compounds tested produced irritation of the conjunctiva early in the study, but the level of severity did not meet the criteria for positive eye irritants.

* DMSO = Dimethyl Sulfoxide

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ABSTRACT

The primary eye irritation potential of the Holston Compounds (Virgin DMSO*, DMSO Recycle Solvent, and DMSO Evaporator Sludge) was tested by placing these materials in the conjunctival cul-de-sac of rabbit eyes. The study was conducted in compliance with the Good Laboratory Practice Regulations. All of the DMSO compounds tested produced irritation of the conjunctiva early in the study, but the level of severity did not meet the criteria for positive eye irritants.

*DMSO = Dimethyl Sulfoxide

PREFACE

TYPE REPORT: Primary Eye Irritation GLP Report

TESTING FACILITY: U.S. Army Medical Research and Development Command
Letterman Army Institute of Research
Division of Research Support
Presidio of San Francisco, CA 94129

SPONSOR: U.S. Army Medical Research and Development Command
U.S. Army Medical Bioengineering Research and Development Laboratory
Fort Detrick, Frederick, MD 21701

PROJECT: DMSO Recrystallization Solution
APC TL01

GLP STUDY NO.: 82036

STUDY DIRECTOR: COL John T. Fruin, DVM, PhD, VC
Diplomate, American College of
Veterinary Preventive Medicine

PRINCIPAL INVESTIGATOR: CPT Craig W. White, DVM, VC

CO-PRINCIPAL INVESTIGATOR: SP4 Thomas P. Kellner, BA

REPORT AND DATA MANAGEMENT: A copy of the final report, study protocols, raw data, retired SOPs, and an aliquot of the test compound will be retained in the LAIR Archives.

TEST SUBSTANCE: The Holston Compounds (Virgin DMSO, DMSO Recycle Solvent, and DMSO Evaporator Sludge).

INCLUSIVE STUDY DATES: 10 February-30 March 1983

OBJECTIVE: The objective of the study is to evaluate the primary eye irritation potential of DMSO recrystallization solvents which are designated Recycle Solvent (TP013), Virgin DMSO (TP014), and Evaporator Sludge (TP015).

ACKNOWLEDGMENTS

The authors wish to thank SP4 Evelyn Zimmerman and Carolyn Lewis, MS, for their assistance in performing the research. Additionally, the authors wish to thank Dr. Jack Dacre and CPT James Carroll of the US Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, MD 21701 for consultation services rendered.

SIGNATURES OF PRINCIPAL SCIENTISTS AND MANAGERS INVOLVED IN THE STUDY:

We, the undersigned, believe the study number 82036 described in this report to be scientifically sound and the results in this report and interpretation to be valid. The study was conducted to comply, to the best of our ability, with the Good Laboratory Practice Regulations for Medical Laboratory Studies, outlined by the Food and Drug Administration.

John T. Fruin 4 May 83
JOHN T. FRUIN / DATE
COL, VC
Study Director

Thomas P. Kellner 4 May 83
THOMAS P. KELLNER, BA / DATE
SP5, USA
Co-Principal Investigator

Craig W. White 4 May 83
CRAIG W. WHITE / DATE
CPT, VC
Principal Investigator

Carolyn M. Lewis 4 May 83
CAROLYN M. LEWIS, MS / DATE
Data Manager

DEPARTMENT OF THE ARMY
LETTERMAN ARMY INSTITUTE OF RESEARCH
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129

REPLY TO
ATTENTION OF:

SGRD-ULZ-QA

7 June 1983

MEMORANDUM FOR RECORD

SUBJECT: Report of GLP Compliance

I hereby certify that in relation to LAIR GLP study 82036 the following inspections were made:

10 Mar 83
16 Mar 83

The report and raw data for this study were audited on 6 June 1983.

Routine inspections with no adverse findings are reported quarterly, thus these inspections are also included in the April 83 report to management and the Study Director.

NELSON R. POWERS, Ph.D.
CPT, MSC
Quality Assurance Officer

TABLE OF CONTENTS

The Holston Defense Corporation has proposed that dimethyl sulfoxide (DMSO) be used as the replacement recrystallization process solvent for HMX/RDX explosive synthesis. As a result of this proposal, a pilot recrystallization facility was put into small scale operation. Samples of the solvent (DMSO) were drawn off at two stages of the process and were designated Recycle Solvent and Evaporator Sludge. These samples may contain major and minor cyclic nitramines which were picked up during the recrystallization process. Because of the extreme tissue penetration properties of DMSO, the U.S. Army Medical Research and Development Command decided that an extensive health hazard assessment would have to be made prior to full-scale munitions production using DMSO as the recrystallization solvent.

The Toxicology Group of Letterman Army Institute of Research was designated by the U.S. Army Medical Research and Development Command to perform the initial toxicological testing on the DMSO samples. The initial data will provide a base for further toxicological testing leading to definitive health protection criteria. These criteria will be used to evaluate facility design and worker protection equipment.

Objective of the Study

The objective of the study is to evaluate the primary eye irritation potential of DMSO recrystallization solvents which are designated Virgin DMSO (TP014), Recycle Solvent (TP013), and Evaporator Sludge (TP015).

METHOD

Test Substances

1. Chemical name: DMSO Recycle Solvent (TP013)

2. Chemical name: Virgin DMSO (TP014)

3. Chemical name: DMSO Evaporator Sludge (TP015)

Chemical data are given in Appendix A.

Animal Data

Animal data appear in Appendix B.

Environmental Conditions

Environmental conditions are described in Appendix C.

Dosing

The nine rabbits were weighed, randomized, and examined. Fluorescein dye and ultraviolet light were used to determine any pre-existing corneal damage 24 hours before the application of the test chemical. No eye lesions were observed.

Three rabbits were assigned to a group for each test chemical. Each rabbit was secured in a restraint cage and the test substance was placed in the right eye of each animal by gently pulling the lower lid away from the eyeball (conjunctival cul-de-sac) to form a cup into which 0.1 ml of liquid was placed. The eyelids were then held together gently to prevent immediate loss of the chemical. The other eye, remaining untreated, served as the negative control. The animals were observed at 1 hour, 24 hours, 48 hours, 72 hours, 4 days, 7 days, 10 days, and 14 days after exposure.

Rationale for Using the Test

The use of animal eyes as test subjects for pharmacological and toxicological examination has been a well-established procedure for a number of years (1). According to earlier technics, six to nine albino rabbits per test chemical were used (2). The U.S. Interagency Regulatory Liaison Group suggests that a trial test be conducted on three rabbits per test substance, and if the substance produced a positive reaction (corrosion, severe irritation) or a negative reaction (slight or no irritation), then no further testing is necessary (3). If equivocal results occur, three more rabbits are tested.

Before and after chemical exposure, ocular reactions are scored with the unaided eye (4). Observations and scoring are conducted according to Table 1 (3). The eyes of all rabbits are further examined after applying fluorescein stain. After flushing out the excess fluorescein with physiological saline, injured areas or the cornea appear green under ultraviolet light.

Any additional observations, such as pannus, phlyctena, rupture of the globe, and vascularization of the cornea, are reported. The grades of ocular reaction are recorded at each examination.

Method of Analysis: Ulceration of the cornea (other than fine stippling), opacity of the cornea (beyond just slight dulling), inflammation of the iris (other than slight deepening of the rugae or light hyperemia of circumcorneal blood vessels), or obvious swelling of the eyelids accompanied by severe conjunctival redness were considered to be signs of positive eye irritation (4).

Duration of Study

A list of historical events appears in Appendix D.

Deviations From Original Protocol

None.

TABLE 1
GRADES FOR OCULAR LESIONS

CORNEA

Opacity: degree of density (area dense taken for reading)
No ulceration or opacity.....0

Scattered or diffuse areas of opacity (other than slight dulling of normal luster, details of iris clearly visible.....1*

Easily discernible translucent areas, details of iris slightly obscured.....2

Nacreous areas, no details of iris visible, size of pupil barely discernible.....3

Opaque cornea, iris not discernible through opacity.....4

IRIS

Normal.....0

Markedly deepened rugae, congestion, swelling, moderate circumcorneal hyperemia or injection, any of these or any combination thereof, iris still reacting to light (sluggish reaction is positive).....1*

No reaction to light, hemorrhage, gross destruction (any or all of these).....2

CONJUNCTIVAE

Redness (refers to palpebral and bulbular conjunctivae excluding cornea and iris)

Blood vessels normal.....0

Some blood vessels difinitely hyperemic (injected).....1

Diffuse, crimson color, individual vessels not easily discernible....2*

Diffuse beefy red.....3

Chemosis: lids and/or nictitating membranes

No swelling.....0

Any swelling above normal (including nictitating membranes).....1

Obvious swelling with partial eversion of lids.....2*

Swelling with lids about half-closed.....3

Swelling with lids more than half-closed.....4

*Indicates minimum level for a positive response (3)

RESULTS

The scale used for scoring appears in Table 1. Tabular scoring data appear in Appendix E.

TP013

Of the three animals tested in this group, none showed signs of corneal opacity or iritis (Tables 1 and 2). Slight conjunctival redness (score of 1) was seen in rabbit 83F107 at the 1-hour observation and in 83F103 at the 1 and 24-hour observations (Table 3). Slight conjunctival chemosis was observed in all rabbits 1-hour after dosing, and these symptoms persisted to 24 hours in animals 83F099 and 83F103 (Table 4).

TP014

None of the three animals tested in this group showed signs of corneal opacity or iritis (Tables 5 and 6). Slight conjunctival redness was seen in all rabbits at the 1-hour observation (Table 7). Conjunctival chemosis was observed for all animals in this group at the 1-hour observation at a severity level of 2 (swelling with partial eversion of the eyelids (Table 8)). All animals showed a marked decrease in chemosis by the next observation period (animal 83F094 showed no chemosis). Animal 83F110 showed scores of 1 from the 24-hour to the 72-hour observation, while 83F104 showed scores of 1 at the 24-hour and 10 day observation periods.

TP015

As with TP013 and TP014, none of the animals tested in this group showed signs of corneal opacity or iritis (Tables 9 and 10). Conjunctival redness was seen in one animal (83F111) at the 1-hour observation (Table 11). Conjunctival chemosis was observed in animal 83F102 at the 1-hour observation and in 83F111 at the 1-hour and 24-hour observation periods (Table 12).

DISCUSSION

In this study a positive reaction is defined as an animal exhibiting one or more of the following signs (above a given level of severity): ulceration of the cornea, opacity of cornea, inflammation of the iris and an obvious swelling of the conjunctiva (accompanied by redness).

Based on these criteria, TP013 and TP015 clearly did not qualify as positive ocular irritants. TP014 did produce scores of 2 for conjunctival chemosis in each rabbit 1 hour after dosing, but this level of severity did not persist to the next day and was not accompanied by severe conjunctival redness. Further, TP014 produced no ulceration of cornea, opacity of the cornea, or inflammation of the iris. Based on these data, TP014 did not qualify as a positive ocular irritant.

CONCLUSION

All three of the DMSO recrystallization process solvents were only slightly irritating to ocular tissues and are classified as negative ocular irritants.

RECOMMENDATION

None.

REFERENCES

1. Hazelton LW. Relation of surface active properties to irritation of the rabbit eye. Toilet Goods Assoc 1952 17:5-9.

2. Draize JJ, Kelly EA. Surface active agents and the eye. Drug Cosmetic Ind 1952; 71:36-37.

3. U.S. Interagency Regulatory Liaison Group. Acute eye irritation testing. 1981.

4. Editorial Committee on Food and Drug Officials of the United States. Appraisal of the safety of chemicals in foods, drugs, and cosmetics. 1959. Association of Food and Drug Officials of the U.S.

Page

APPENDICES

Toxicity Test Sample Composition*

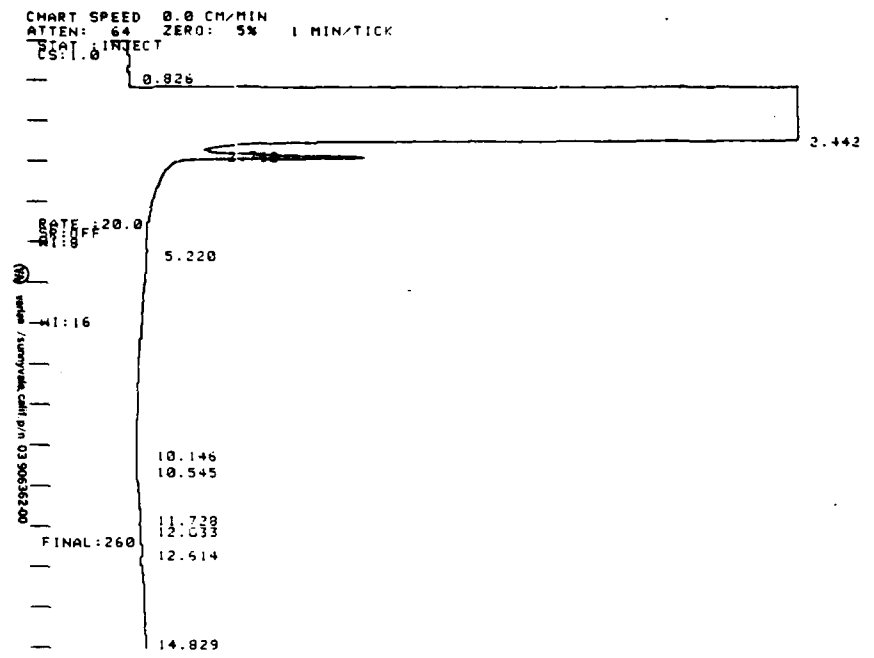
Sample	Concentration by HPLC, g/l RDX	HMX	TAX	SEX	%H_2O (3)	%DMSO
Virgin DMSO (1)	0	0	0	0	0.63	99.37
DMSO Recycle Solvent (2)	24.188	39.542	0.263	0	35.48 (4)	58.64 (5)
DMSO Evaporator Sludge (1)	0.548	0.942	3.521	0	5.35 (4)	94.19 (5)

(1) At ambient temperature.
(2) Analysis of equilibrium liquid at 40 C.
(3) By Karl Fisher
(4) Water content calculated by difference.
(5) DMSO content by gas chromatography using virgin DMSO sample as the standard.

Calculated Data In Weight Percent

Sample	RDX	HMX	TAX	SEX	H_2O	DMSO
Virgin DMSO	0	0	0	0	0.63	99.37
DMSO Recycle Solvent	2.22	3.64	0.02	0	35.48	58.64
DMSO Evaporator Sludge	0.05	0.09	0.32	0	5.35	94.19

*Data supplied by sponsor



TITLE: 10:29 31 MAR 83

CHANNEL NO: 1 SAMPLE: "SLUDGE" METHOD: THIOLS

PEAK NO	PEAK NAME	RESULT AREA %	TIME (MIN)	TIME OFFSET	AREA COUNTS	SEP CODE	WI/2 (SEC)
1		65.3886	5.220		8169	BB	? 15.60
2		34.6114	11.728		4324	VV	? 27.00
TOTALS:		100.0000			12493		

DETECTED PKS: 13 REJECTED PKS: 11

MULTIPLIER: 1.00000

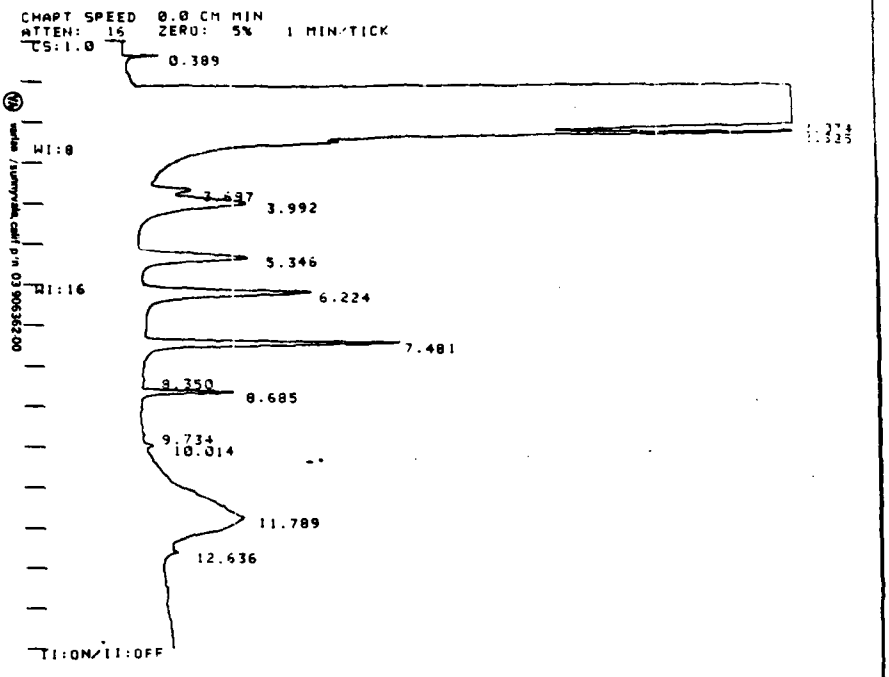
NOISE: 0.0 OFFSET: -0

SAVED FILE: RDX006

NOTES:
COL: 2 M GLASS - 5% OV-17, 80-100 MESH
CARRIER: NITROGEN - 20 ML/MIN
INJ: 150° C DET: 270° C
TEMP PROG: 100° TO 260° C @ 20°C/MIN
SOLVENT: DMSO SAMP SIZE: 0.5 UL
DETECTOR: FID - SENSITIVITY: 10-10
RUN LENGTH: 15 MINUTES

Gas Chromatograph Analysis of DMSO Evaporator Sludge

APPENDIX A (cont.)



141

RECALC
TITLE:

12:13 29 MAR 83

CHANNEL NO: 1 SAMPLE: TP013 METHOD: THIOLS

PEAK NO	PEAK NAME	RESULT AREA %	TIME (MIN)	TIME OFFSET	AREA COUNTS	SEP CODE		WI/2 (SEC)
1		12.4597	5.346		35291	BV		12.50
2		19.7905	6.224		56055	VV		10.70
3		17.5359	7.481		49669	VV		6.75
4		4.2547	8.685		12051	VB	?	3.10
5		44.8299	11.789		126977	VV	?	53.15
6		1.1294	12.636		3199	VB	?	6.40
TOTALS:		100.0000			283242			

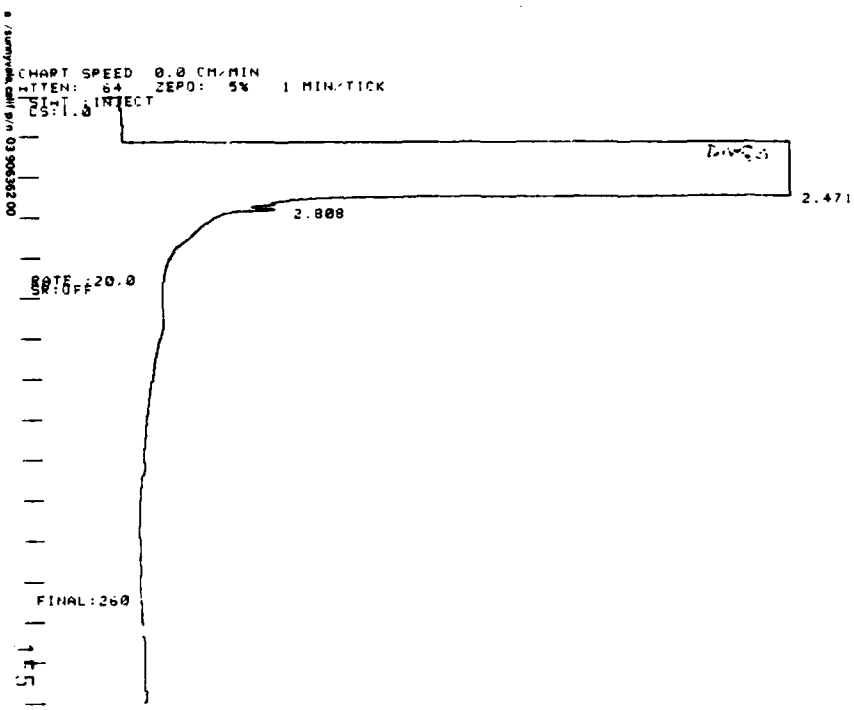
DETECTED PKS: 15 REJECTED PKS: 9

MULTIPLIER: 1.00000

NOISE: 1.2 OFFSET: -5

NOTES:
COL: 2 M GLASS - 5% OV-17, 80-100 MESH
CARRIER: NITROGEN - 20 CC/MIN
INJ: 150° C DET: 270° C
TEMP PROG: 100° TO 260° @ 20°C/MIN
SOLVENT: DMSO ? SAMP SIZE: 1 UL
DETECTOR: FID - SENSITIVITY 10-10
RUN LENGTH: 15 MINUTES

Gas Chromatograph of DMSO Recycle Solvent



TITLE: 9:26 31 MAR 82

CHANNEL NO: 1 SAMPLE: DMSO METHOD: THIOLS

PEAK NO	PEAK NAME	RESULT AREA %	TIME (MIN)	TIME OFFSET	AREA COUNTS	SEP CODE	WI/2 (SEC)
TOTALS:		0.0000			0		

DETECTED PKS: 4 REJECTED PKS: 4

MULTIPLIER: 1.00000

NOISE: 2.4 OFFSET: -4

SAVED FILE: PD-003

ERRORS:
NO PEAKS

NOTES:
COL: 2 M GLASS - 5% OV-17, 80-100 MESH
CARRIER: NITROGEN - 20 ML/MIN
INJ: 150° C DET: 270° C
TEMP PROG: 100° TO 260° C @ 20°C/MIN
SOLVENT: DMSO SAMP SIZE 1UL
DETECTOR: FID - SENSITIVITY: 10-10
RUN LENGTH: 15 MINUTES

Gas Chromatograph Analysis of Virgin DMSO

APPENDIX A (concluded)

ANIMAL DATA

Species: Rabbit

Strain: New Zealand White (albino)

Source: Elkhorn Rabbitry
5265 Starr Way
Watsonville, CA 95076

Sex: Male

Age: Young adults

Method of randomization: RANDOM Program on eclipse C330 computer (SOP OP-ISG-21).

Animals in dose group: 3 (3 groups)

Condition of animals at start of study: Normal

Body weight range: 2405-2977 g; $\bar{x}$ = 2669; s = 197

Identification procedures: Ear tattoo (SOP-OP-ARG-1)

Pretest conditioning:

1. Quarantine from 10 February-24 February 1983

2. Animal eyes were examined 24 hours before dosing using fluorescein dye and ultraviolet light.

Justification: Rabbits are a proven sensitive animal model for this test

ENVIRONMENTAL DATA

Caging: Number/cage = 1; type of cage = stainless steel, wire mesh bottom, battery type, no bedding, automatic flush.

Diet: Purina Certified Rabbit Chow No. 5322, approximately 110 g/day, Lot No. SEPT09822A and JAN06831A

Water: Central line to cage battery with automatic lick dispensers.

Temperature: 72 $\pm$ 5°F (22 $\pm$ 2°C (temperature and relative humidity did excees the stated limits for approximately 1 hour on 12 and 13 March 1983. No adverse reactions were exhibited by these animals).

Relative Humidity: 56 $\pm$ 10%

Photoperiod: 0530-2000 hours per day (light 14-1/2 hours)

HISTORICAL LISTING OF STUDY EVENTS

Date	Day	Event
10 Feb 83	A 0	Rabbits arrived at LAIR. They were weighed, tatooed (SOP OP-ARG-1), checked for illness, and quarantined by ARG for 2-3 weeks.
24 Feb 83	A 14	Animals were removed from quarantine.
25 Feb 83	A 15	Animals were weighed.
4 Mar 83	A 22	Animals were weighed.
8 Mar 83	A 26	Rabbits were randomized and checked for pre-existing ocular injury.
9 Mar 83	0	Rabbits were dosed according to test chemical group and weighed. 1 hour after exposure eyes were observed and scored.
10 Mar 83	1	24 hours after exposure eyes were observed and scored.
11 Mar 83	2	48 hours after exposure eyes were observed and scored.
12 Mar 83	3	72 hours after exposure eyes were observed and scored. Animals were weighed.
13 Mar 83	4	4 days after exposure eyes were observed and scored.
16 Mar 83	7	7 days after exposure eyes were observed and scored. Animals were weighed.
14-23 Mar 83	5-14	Rabbits were observed daily if scores were not performed.
19 Mar 83	10	10 days after exposure eyes were observed and scored.
23 Mar 83	14	14 days after exposure eyes were observed and scored. Animals were weighed.
30 Mar 83	21	Animals were removed from the study.

APPENDIX D

TABULAR SCORING DATA
ON
ACUTE EYE IRRITATION SUMMARY FORMS

TABLE 1

Acute Eye Irritation Summary

Rabbits

Area Summarized Cornea

GLP Study No. 82036 Chemical Name TP013

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F099	0	0	0	0	0	0	0	0
83F103	0	0	0	0	0	0	0	0
83F107	0	0	0	0	0	0	0	0

APPENDIX E

TABLE 2

Acute Eye Irritation Summary

Rabbits

Area Summarized Iris

GLP Study No. 82036 Chemical Name TP013

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F099	0	0	0	0	0	0	0	0
83F103	0	0	0	0	0	0	0	0
83F107	0	0	0	0	0	0	0	0

TABLE 3

Acute Eye Irritation Summary

Rabbits

Area Summarized Conjunctiva (redness)

GLP Study No. 82036 Chemical Name TP013

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F099	0	0	0	0	0	0	0	0
83F103	1	1	0	0	0	0	0	0
83F107	1	0	0	0	0	0	0	0

TABLE 4

Acute Eye Irritation Summary

Rabbits

Area Summarized Conjunctiva (chemosis)

GLP Study No. 82036 Chemical Name TP013

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F099	1	1	0	0	0	0	0	0
83F103	1	1	0	0	0	0	0	0
83F107	1	0	0	0	0	0	0	0

APPENDIX E (cont.)

TABLE 5

Acute Eye Irritation Summary

Rabbits

Area Summarized Cornea

GLP Study No. 82036 Chemical Name TP014

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F094	0	0	0	0	0	0	0	0
83F110	0	0	0	0	0	0	0	0
83F104	0	0	0	0	0	0	0	0

TABLE 6

Acute Eye Irritation Summary

Rabbits

Area Summarized Iris

GLP Study No. 82036 Chemical Name TP014

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F094	0	0	0	0	0	0	0	0
83F110	0	0	0	0	0	0	0	0
83F104	0	0	0	0	0	0	0	0

TABLE 7

Acute Eye Irritation Summary

Rabbits

Area Summarized Conjunctiva (redness)

GLP Study No. 82036 Chemical Name TP014

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F094	1	0	0	0	0	0	0	0
83F110	1	0	0	0	0	0	0	0
83F104	1	0	0	0	0	0	0	0

TABLE 8

Acute Eye Irritation Summary

Rabbits

Area Summarized Conjunctiva (chemosis)

GLP Study No. 82036 Chemical Name TP014

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F094	2	0	0	0	0	0	0	0
83F110	2	1	1	1	0	0	0	0
83F104	2	1	0	0	0	0	1	0

TABLE 9

Acute Eye Irritation Summary

Rabbits

Area Summarized Cornea

GLP Study No. 82036 Chemical Name TP015

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F097	0	0	0	0	0	0	0	0
83F102	0	0	0	0	0	0	0	0
83F111	0	0	0	0	0	0	0	0

TABLE 10

Acute Eye Irritation Summary

Rabbits

Area Summarized Iris

GLP Study No. 82036 Chemical Name TP015

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F097	0	0	0	0	0	0	0	0
83F102	0	0	0	0	0	0	0	0
83F111	0	0	0	0	0	0	0	0

TABLE 11

Acute Eye Irritation Summary

Rabbits

Area Summarized Conjunctiva (redness)

GLP Study No. 82036 Chemical Name TP015

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F097	0	0	0	0	0	0	0	0
83F102	0	0	0	0	0	0	0	0
83F111	2	0	0	0	0	0	0	0

TABLE 12

Acute Eye Irritation Summary

Rabbits

Area Summarized Conjunctiva (chemosis)

GLP Study No. 82036 Chemical Name TP015

Principal Investigator White/Kellner Physical State Liquid

Date Started 9 Mar 83 Amount Applied 0.1 ml

Score by Animal

Rabbit No.	1 hr	24 hr	48 hr	72 hr	4 d	7 d	10 d	14 d
83F097	0	0	0	0	0	0	0	0
83F102	1	0	0	0	0	0	0	0
83F111	2	1	0	0	0	0	0	0

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